IN THE UNITED STATES DISTRICT COURT FOR THE
MIDDLE DISTRICT OF TENNESSEE
NASHVILLE DIVISION

RUTH SMITH, Individually and as Widow for the Use and Benefit of Herself and the Next Kin of Richard Smith, Deceased,	)	
Plaintiff,	)	Civil No. 3:05-0444
	)	Judge Aleta A. Trauger
v.	)	(Dist. Of MA No.
	)	1:05-cv-11515PBS)
PFIZER, INC., *et al.*,	)	
Defendants.	)	

DEFENDANTS' OPPOSITION TO PLAINTIFF'S MOTION *IN LIMINE* TO PRECLUDE ANY TESTIMONY OR DISCUSSION BY DEFENDANTS THAT THEY COULD NOT HAVE AMENDED THE NEURONTIN LABEL OR ISSUED STRENGTHENED WARNINGS WITHOUT PRIOR FDA APPROVAL

Defendants Pfizer Inc and Warner-Lambert Company LLC (collectively, "Defendants" or "Pfizer") hereby respond to Plaintiff's motion *in limine* to preclude Pfizer from arguing that it could not have amended the Neurontin label without prior approval of the Food and Drug Administration ("FDA") and respectfully request that the Court deny the motion to the extent it seeks to preclude Pfizer from presenting evidence about the reasonableness of its conduct.

During the final pretrial hearing in *Bulger v. Pfizer Inc.*, 1:04-10981-PBS, the MDL court addressed a substantially identical motion *in limine* filed by the plaintiff in that case, who was also represented by the same counsel. [MDL Docket Nos. 1881, 1883] The MDL court noted that the plaintiff's motion was "just a legal argument" – the implication being that it was not an issue appropriately addressed in a motion *in limine*. (Ex. A, Final Pretrial Conference Transcript, *Bulger*, at 55:14-17.)[1] The MDL court then agreed with Pfizer's stance that evidence related to showing the context surrounding its decision regarding the Neurontin label was admissible. (*Id.* at 56:1-13.) For the sake of completeness and clarity, that stance is reasserted below.

[1] All exhibits are attached to the accompanying Declaration of Mark S. Cheffo.

The adequacy of Pfizer's warning is directly at issue in this litigation. Indeed, unless Plaintiff can prove that Pfizer was negligent by not including a suicide warning in the 2004 Neurontin label, Plaintiff's claim fails. The fact that the FDA had approved the specific language in the label and the fact that the FDA could reject any proposed labeling change, even one made pursuant to the "changes being effected" procedure, is clearly relevant to whether Pfizer behaved as a reasonable manufacturer.

Pfizer does not intend to make legal arguments to the jury. Rather, Pfizer will direct such arguments to the Court and will rely upon the Court to instruct the jury as to the applicable law. Pfizer is, however, entitled to put the reasonableness of its conduct into context. It must be permitted, for example, to present expert testimony on whether or not it would have been reasonable for Pfizer to have included in the Neurontin labeling, at the time that Richard Smith was prescribed Neurontin, a warning that Neurontin can increase the risk of suicidal thoughts or behavior. This testimony will, among other things, address the many reasons why a manufacturer would not want to make this unilateral change to a label and should not warn of risks in the absence of sufficient scientific and medical evidence, as well as the responsibility of the FDA to accept or reject the labeling change under the applicable regulations.

As Plaintiff concedes, although a pharmaceutical manufacturer may, through a "changes being effected" or "CBE" supplement, make certain changes to product labeling without prior FDA approval in order "to reflect newly acquired information," 21 C.F.R. § 314.70(c)(6)(iii), a CBE revision may be temporary as the FDA retains final authority to accept or reject the labeling change. *See* 21 C.F.R. § 314.70(c)(7); *Wyeth v. Levine*, 129 S. Ct. 1187, 1198 (2009); *see also* 21 C.F.R. § 314.3(b) (defining "newly acquired information"). As the FDA explained in the Final Rule amending the CBE regulation to clarify that, for purposes of a CBE label change, the "newly acquired information" on which such a change is based "needs to be of a different type or greater severity or frequency than previously included in submissions to FDA": "This amendment . . . is intended to ensure that scientifically valid and appropriately worded warnings will be provided in the approved labeling for medical products, and to prevent overwarning,

which may deter appropriate use of medical products, or overshadow more important warnings." Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, Final Rule, 73 Fed. Reg. 49,603-01, at 49,604-06, 2008 WL 3874230 (Aug. 22, 2008) (internal quotation marks omitted); *see also id.* at 49,608 ("[T]he purpose of the final rule is to clarify that a CBE supplement is appropriate to amend the labeling for an approved product only to reflect newly acquired information, and to clarify that a CBE supplement may be used to add or strengthen a contraindication, warning, precaution, or adverse reaction only if there is reasonable evidence of a causal association with the approved drug, biologic, or medical device.").[2]

Thus, as the very regulation on which Plaintiff relies confirms, limiting the evidence and argument at trial to that establishing that Pfizer could have changed its warning label without advance FDA approval would be misleading and prejudicial. The jury is entitled to learn, for example, of the CBE requirement and definition of newly acquired information and of the FDA's authority to prevent such changes from becoming permanent. In addition, Pfizer should be permitted to establish, through expert testimony, the nature of the CBE process and the FDA's active role once the process is undertaken. This is especially true here, where the FDA: (1) had considered Neurontin data on depression and suicide on multiple occasions and had never, before December 2008, required that Pfizer include a warning about suicidal behavior in Neurontin's label; (2) did so then based only on *pooled* data from eleven drugs; and (3) had expressly required that language regarding the proposed mechanism of action on which Plaintiff's experts rely, that is, that Neurontin reduces the release of noradrenaline, dopamine, and glutamate under certain laboratory conditions, be *deleted* from the label. (*See, e.g.*, Ex. C, Aff. of Cynthia McCormick, M.D., ¶¶ 40-41.)

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[2] Warnings about off-label use, such as that at issue in the instant case, are subject to additional FDA regulations. *See* 21 C.F.R. § 201.57(c)(2)(ii). In addition, as the FDA's approval letters for Neurontin explicitly stated, "[t]he final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug." (Ex. B, 2002 Approval Letter.)

Pfizer must be permitted to present expert testimony that, under these circumstances, it was reasonable that Pfizer would not have unilaterally changed its label pursuant to the CBE regulations before Neurontin was last prescribed to Mr. Smith. Such testimony would be presented not to establish what Pfizer legally could or could not have done under FDA regulations, but what was reasonable for it to have done. *Wyeth v. Levine*, on which Plaintiff relies, stands for the proposition that FDA approval of a drug's labeling does not create an absolute legal defense to a failure-to-warn claim. *See* 129 S. Ct. at 1204. It does not support a finding that a defendant should be prohibited from presenting, and juries from considering, factors proffered by a competent expert that would make it reasonable or unreasonable for a manufacturer to submit a CBE supplement to warn of a particular risk.

For the foregoing reasons, Pfizer respectfully requests that the Court deny Plaintiff's motion to the extent it seeks to preclude Pfizer from presenting evidence about the reasonableness of its conduct in the context of the FDA regulatory regime.

Dated: April 27, 2010

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on this the 27th day of April 2010, I electronically filed the foregoing document with the Clerk of the Court, United States District Court for the Middle District of Tennessee, using the CM/ECF system. True and correct copies of the foregoing documents are being served via the Court's CM/ECF system on the following:

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